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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,105	10/04/2001	Ann Burchell	350013-76	4877

20995 7590 02/09/2005

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,105	BURCHELL ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/23/04* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/392,055.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/23/04 has been entered.

2. Applicants' response to the Final Office Action mailed September 24, 2003 is acknowledged. In response to amendment filed therein, claims 1, 8, 10, 11, and 16-23 have been canceled and claims 2, 7, 9, and 12 were modified. Currently, claims 2-7, 9, and 12-15 are under consideration.

3. Rejections and/or Objections of record not reiterated herein have been withdrawn.

OBJECTIONS MAINTAINED

Drawings

4. The drawings in this application are objected to by the Draftsperson as informal. Any drawing corrections requested, but not made in the prior application should be repeated in this application if such changes are still desired.

If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Also, Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Applicants have indicated that formal drawings were submitted(response filed 1/23/04 on page 6), however the photos are not available for consideration. Please re-submit the photos. Applicant will file petition and formal drawings to correct the noted deficiencies. Until receipt and subsequent approval of the drawings the objection is maintained.

REJECTIONS WITHDRAWN

Double Patenting

5. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 2, 6, 9, 10, and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 6,331,395.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to methods of isolating embryonic or fetal red blood cells via antibodies to GLUT2 (glucose transporter 2). Specifically the instant claims (2, 6, 9, 10, and 12) are drawn to a broad method of isolating embryonic or fetal red blood cells that encompasses the particular GLUT2 (glucose transporter 2) of claim 1 in patent #6,331,395. Accordingly the instant invention is encompassed in US Patent #6,331,395. It would have been obvious to the skilled practitioner in the art to employ various known adult liver components in the method of isolating embryonic or fetal red cells as an obvious modification of the known method in patent 6,331,395 because it has been held that the provision of adjustability, where needed, involves only routine skill in the art. *In re Stevens*, 101 USPQ 284 (CCPA 1954).

Response to Argument

7. The terminal disclaimer filed on 6/3/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent #6,331,395 has been reviewed and is accepted. The terminal disclaimer has been recorded. Accordingly, the rejection under obvious double patenting is withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 14 and 15 are vague and indefinite because they are dependent on canceled claim 10. Accordingly, it is not clear if Applicant intends to cancel the limitations of claims 14 and 15? Is it Applicants intent to have claims 14 and 15 dependent on another claim? Appropriate correction is required.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 2, 5-7, 9 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770).

Bianchi et al. teach a method of isolating fetal nucleated cells from maternal blood. An antigen present on the cell surface of the fetal erythrocyte is detected and related to a gene or gene portion associated with a disease or condition, a chromosomal abnormality or sex-specific DNA, in the maternal blood sample. See abstract.

Three different antibodies are utilized to separate the fetal nucleated erythrocytes (red blood cells) form maternal blood. These antibodies are anti-CD 71, anti-CD 36, and anti-GPA. Anti-CD 71 binds the transferrin receptor, CD-36 binds the thrombospondin receptor (hormone receptor), while anti-GPA binds glycophorin A. See page 294 4th paragraph. Blood samples were collected from pregnant women between 8 and 19 weeks gestation (within the first trimester). See page 295 1st paragraph.

The method is cells were isolated/separated by antibody binding and analyzed via flow cytometry, sorting, and PCR. See page 295 through 296. The results showed that the GPA (red cell-specific antigen) allowed for the separation of fetal nucleated erythroid cells from maternal blood. See page 299 last paragraph.

Bianchi et al. differs from the instant invention in failing to teach a method of identifying and isolating embryonic or fetal red blood cells via an adult liver component that is cell surface exposed.

It is noted that the specification teaches that glucose-6-phosphase is an adult liver component meeting the limitations of the claims. (Page 8 section 0047). The references to Hume et al. disclose the use of antibodies to glucose-6-phosphase.

Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) show that the microsomal glucose-6-phosphatase enzyme protein is expressed in human embryonic and fetal red blood cells. Glucose-6-phosphatase was found to be immunopositive for circulating red cells in the primitive megaloblastic series.

Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) et al. teaches that microsomal glucose-6-phosphatase catalyzes the terminal step of glycogenolysis and gluconeogenesis and is expressed predominantly in the liver. The study of the endoplasmic reticulum system involving glucose-6-phosphatase, lead investigators to study other endoplasmic reticulum proteins. These proteins included uridine diphosphate-glucuronosyltransferase, cytochrome P450 isozymes, nicotinamide adenine dinucleotide phosphatecytochrome P450 oxidoreductase, and prostaglandin H synthase.

Bianchi et al., Hume et al., and Hume et al., are all analogous art because they are from the same field of endeavor, all three inventions teach immunoassay techniques involving fetal red blood cells and prenatal diagnosis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the specific proteins relating to microsomal glucose-6-phosphatase as taught by Hume et al., and Hume et al. in the methods of Bianchi et al. to perform fetal red blood cell identification, isolation, and assay techniques, because Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) taught that the predominantly hepatic protein (glucose-6-phosphatase) in adults is present in nucleated embryonic and fetal red blood cells and is useful in diagnosis of disorders associated with liver protein expression in the first trimester maternal circulation.

While, Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) taught that expression of these key enzymes (glucose-6-phosphatase) in early fetal RBCs provides a means for the study of fetal development in these areas. See abstract.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible treatment and early preparation/education of the fetal family for the birth of an abnormal baby.

With respect to claim 7 wherein the concentration of the detectable adult liver component is at less than 1 percent per cell basis in maternal cells. Such detection limits are viewed as mere assay optimization. Absent results to the contrary or unexpected results the modification is viewed as an obvious modification that does not render the claims patentably distinct from the prior art assay methods.

II. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al. (Prenatal Diagnosis, Vol.13, 293-300, 1993) in view of Hume et al. (Early Human Development, Vol.42, No.2, 1995, pp. 85-95) and Hume et al. (Blood, Vol.87, No.2, 1996, pp.762-770) as applied to claims 2, 5-7, 9 and 14-15 above, and further in view of in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Bianchi et al. in view of Hume et al. and Hume et al. as set forth above.

Bianchi et al. in view of Hume et al. and Hume et al. differ from the instant invention in not specifically teaching reagent immobilization to a solid support such as micro titer plates.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the reagents on a solid support/micro titer plates as taught by Maggio in the assay method to isolate red blood cells of Bianchi et al. in view of Hume et al. and Hume et al. because Maggio taught that micro plates or micro titer plates "are very convenient for reagent immobilization and eliminate washing thereby reducing labor in assay procedures". Page 186, last line.

Response to Arguments

10. Applicant contends that Bianchi et al. (WO 91/07660) and Spector et al. (Am J Hum Genet. 32;79-87,1980) do not teach the instant invention because they do not measure an adult liver component as defined by the claims and their combination with the references of Hume et al. were improper. This argument was carefully considered and found persuasive. The previously cited reference of Bianchi et al. and Spector et al. have been withdrawn.

A newly cited reference to Bianchi et al. (Prenatal Diagnosis, 13, 293-300, 1993) has been cited in combination with the references to Hume et al. While a deficiency in a reference may overcome a rejection under 35 USC 103, a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F2d 1005, 150 USPQ 741, 746 (CCPA 1966).

In response to the argument that the references of Hume et al. teach away from the instant invention because they do not relate to the isolation of fetal cells, it is noted that the Hume et al. references teach the detection of fetal cells (containing primitive megaloblastic nucleated red cells) by binding with the glucose-6-phosphatase in fetal tissue, embryos, and blood sampling. These cells are decrease after 12 weeks gestation (less than 5%). Embryos and fetal tissues would also contain cells from the maternal circulation. The maternal cells do not contain primitive megaloblastic nucleated red cells, accordingly the fetal cells would be isolated by virtue of being detected by glucose-6-phosphatase. See Hume et al. abstracts.

In response to the argument that the references are non-analogous, it is noted that all the references are directed to the detection of nucleated red blood cells.

In response to the argument regarding the characterization of glucose-6-phosphatase (intra-cellular vs. cell surface), it is noted that the specification teaches glucose-6-phosphatase on page 8 section 0047 through page 9 section 0048. The antibody taught by Hume et al. would detect glucose-6-phosphatase regardless of where it is expressed (intra-cellular or cell surface).

Because the component exits in either state (cell surface exposed or intra cellular component) absent evidence to the contrary, this limitation is deemed obvious to the detected complex (glucose-6-phosphatase). Since it has been held that the provision of adjustability, where needed, involves only routine skill in the art. *In re Stevens*, 101 USPQ 284 (CCPA 1954).

Applicant argues that the examiner has applied an "obvious to try standard." An "obvious to try" standard is deemed impermissible in two situations: 1) where the prior art gives no indication as to which of numerous parameters are critical, or give no indication as to which of many possible choices is likely to be successful; and 2) where the prior art gives only general guidance with respect to the form of the invention, but not how to achieve it in new areas of technology or in fields of experimentation which are only seemingly promising. In re O'Farrell, 853 F.2d 894, 7 USPQ 2d 1673, 1681 (Fed Cir 1988).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to the argument that the rejection of claim 13 in further view of Maggio is not obvious by virtue of its dependency on amended claims 2 and 9, it is noted that the primary references have been addressed above. Accordingly the rejection of claim 13 has been modified Above.

11. For reasons aforementioned, no claims are allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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